HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN
FOR
N-ETHYL-N-(3-METHYLPHENYL)-1,2-ETHANEDIAMINE
(CAS NO.: 19248-13-6)

PREPARED BY:

EASTMAN CHEMICAL COMPANY

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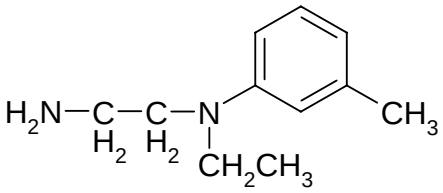
OVERVIEW

The Eastman Chemical Company hereby submit for review and public comment the test plan for N-ethyl-N-(3-methylphenyl)-1,2-ethanediamine (EMPE; CAS NO.: 19248-13-6) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. It is the intent of our company to use existing data on EMPE in conjunction with EPA-acceptable predictive computer models to adequately fulfill the Screening Information Data Set (SIDS) for the physicochemical, environmental fate, ecotoxicity test, and human health effects endpoints. In addition, we believe that due to the sole use of this material as an industrial intermediate used solely on-site in a closed system manufacturing process a reduced set of data are needed. Thus, in total the submitted data are adequate to fulfill all the requirements of the HPV program without need for the conduct any new or additional tests.

TEST PLAN SUMMARY

CAS No. 19248-13-6 	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Required
STUDY	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL DATA							
Melting Point	Y	-	Y	-	N	Y	N
Boiling Point	Y	-	Y	-	N	Y	N
Vapor Pressure	Y	-	-	Y	N	Y	N
Partition Coefficient	Y	-	-	Y	N	Y	N
Water Solubility	Y	-	-	Y	N	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	-	-	Y	N	Y	N
Stability in Water	Y	-	-	Y	-	Y	N
Biodegradation	Y	Y	-	-	Y	Y	N
Transport between Environmental Compartments (Fugacity)	Y	-	-	Y	N	Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	Y	-	-	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	-	-	Y	Y	N
Toxicity to Aquatic Plants	Y	Y	-	-	Y	Y	N
TOXICOLOGICAL DATA							
Acute Toxicity	Y	N	Y	-	N	Y	N
Repeated Dose Toxicity	N	-	-	-	-	-	N
Genetic Toxicity – Mutation	Y	Y	-	-	Y	Y	N
Genetic Toxicity – Chromosomal Aberrations	Y	Y	-	-	Y	Y	N
Developmental Toxicity	Y	Y	-	-	-	Y	N
Toxicity to Reproduction	N	-	-	-	-	-	N

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical

Melting point - Data for this endpoint were obtained using a measured value and by using a computer estimation-modeling program within EPIWIN(1).

Boiling Point - Data for this endpoint were obtained using a measured value.

Vapor Pressure - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN(1).

Partition Coefficient - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.

Water Solubility - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.

Conclusion: All end points have been satisfied by utilizing data obtained from the various physical chemical data modeling programs within EPIWIN or from use of measured data. Estimation models within EPIWIN have been noted by the Agency as acceptable in lieu of actual data or values identified from textbooks. No new testing is required.

B. Environmental Fate

Photodegradation - A value for this endpoint was obtained using AOPWIN, a computer estimation-modeling program within EPIWIN (1).

Stability in Water - No data are available. A technical discussion describing the stability of EMPE in water has been provided.

Biodegradation - This endpoint was satisfied through the use of a study that followed OECD-301B guidelines and was conducted under GLP assurances.

Fugacity - A value for this endpoint was obtained using the EQC Level III partitioning computer estimation model within EPIWIN.

Conclusion: Except water stability all endpoints have been filled with data utilizing acceptable methodologies and of sufficient quality to fulfill these endpoints. No new testing is required.

C. Ecotoxicity Data

Acute Toxicity to Fish - This endpoint is filled by data from a study that followed OECD TG-203 and was conducted under GLP assurances.

Acute Toxicity to Aquatic Invertebrates - This endpoint is filled by data from a study that followed OECD TG-202 and was conducted under GLP assurances.

Toxicity to Aquatic Plants - This endpoint is filled by data from a study that followed OECD TG-201 and was conducted under GLP assurances.

Conclusion: All endpoints, but algal toxicity, have been satisfied with data from studies that were conducted using established OECD guidelines and GLP assurances. No new testing is required.

D. Toxicological Data

Acute Toxicity - This endpoint is filled by data from studies conducted in rats that assessed the toxicity of EMPE following both oral and inhalation exposures. Although the studies did not follow standardized guideline protocols they were deemed as "reliable with restrictions".

Repeat Dose Toxicity - No data are available other than that which is contained in the OECD 421 developmental and reproductive toxicity screening study. However, the sole use of this material is as a closed system intermediate and arguments are presented to support a reduced set of testing needs that excludes repeat dose toxicity studies.

Genetic Toxicity

Mutation - This endpoint is filled with a study that followed OECD guideline 471 and was conducted under GLP assurances. The quality of this study was deemed as "reliable without restrictions".

Aberration - This endpoint is filled with data from an *in vitro* study using Chinese hamster ovary (CHO) cells that followed OECD guideline 473 and was conducted under GLP assurances. The quality of this study was deemed as "reliable without restrictions".

Developmental

Toxicity - This endpoint is filled by data from an oral exposure study in rats that followed OECD guideline 421 and was conducted under GLP assurances. This protocol evaluates both developmental and reproductive toxicity potential.

Reproductive

Toxicity - No data are available, nor are data needed, due to the nature of the manufacture and use of this compound (i.e., closed system intermediate). Nevertheless, this endpoint is filled by data from an oral exposure study in rats that followed OECD guideline 421 and was conducted under GLP assurances. This protocol evaluates both developmental and reproductive toxicity potential.

Conclusion: All endpoints have been satisfied with data from studies whose methods followed established OECD guidelines and GLP assurances or were conducted using acceptable methodologies.

SIDS DATA SUMMARY

Data assessing the various physicochemical properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility) for EMPE were obtained from estimations using the models within EPIWIN or from measured values. These data indicate that EMPE is a liquid at room temperature (MP <0 ^{o}C) with a low vapor pressure (0.036 hPa at 25 °C) and a boiling point in excess of 250 °C. It has an octanol to water partition coefficient (K_{ow}) of 2.23 and an estimated water solubility of 12,090 mg/L.

The assessment of the environmental fate endpoints photodegradation and biodegradation indicate the material is capable of being degraded by photochemical reactions but appears to not be readily degraded using biological processes and it is hydrolytically stable. Fugacity predictions indicate a very limited amount of partitioning into the air, with >99% estimated to be distributed into the soil (65.7%) and water (34.1%).

The data from the various studies conducted to assess ecotoxicity potential indicate EMPE may be toxic to fish, daphnia, and algae with LC_{50} and EC_{50} concentrations of less than 10 mg/L for all three species.

The acute toxicity of EMPE following oral exposure is moderate as the LD_{50} value was approximately 400 mg/kg in rats and 400 - 800 mg/kg in mice. The LC_{50} value following inhalation exposure to rats is >4.58 mg/L. The material is not genotoxic based on the negative results of an Ames study and an *in vitro* chromosomal aberration study. Data from repeated exposure studies are not deemed necessary due to the nature of the manufacture and use of this material. Data from an OECD 421 developmental and reproductive toxicity screen indicate the material is not a reproductive toxicant. Fetotoxicity manifested as low birth weights was noted at the highest dose of 200 mg/kg. However, the NOAEL for maternal toxicity was 20 mg/kg. No evidence of teratogenic effects were noted.

In conclusion, data to adequately assess all the SIDS endpoints are currently available or will be available. Importantly, due to its only known use as a closed system on-site industrial intermediate with no known direct applications within consumer products, exposure to the general public is not anticipated and exposure to workers is managed through prudent industrial hygiene practices.

JUSTIFICATION TO SUPPORT REDUCED TESTING

It is believed that a reduced set of hazard data are needed for EMPE due to the fact that this compound is a closed-system industrial intermediate used only on-site at one manufacturing facility and is not transported. The documentation for the basis of this claim is detailed in the attached appendix.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general US EPA guidance (2) and the systematic approach described by Klimisch *et al.* (3). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

1. Reliable without Restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

2. Reliable with Restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

3. Not Reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

4. Not Assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

REFERENCES

1. EPIWIN, Version 3.11, Syracuse Research Corporation, Syracuse, New York.

2. USEPA (1998). 3.4 Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.

3. Klimisch, H.-J., Andreae, M., and Tillmann, U. (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regul. Toxicol. Pharmacol.* 25:1-5.